Protein corona characterization through analytical quality-by-design

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Background. After administration of nanoparticles (NP) into biological fluids, the NP may interact with surrounding biomolecules like proteins [1]. Those interactions can then cause protein corona (PC) that affect the physicochemical and biological properties of NP. Numerous studies have been carried out to characterize PC effects in simple and complex biological media but our understanding is far from being complete. Moreover, the variety of methods and tools used for this purpose prevents any robust conclusion and sometimes introduces confusions and uncertainty.
Analytical Quality by Design (AQbD), introduced in 2010 [2], is the application of the QbD concept, strongly recommended by FDA, to analytical method development [3] . AQbD aims at optimizing accuracy and robustness of analysis results by identifying and controlling critical quality variables and risk factors over the complete protocol, including biological sample preparation, metrological protocol and statistical analysis.

Objectives

Our goal is to establish a safe and repeatable protocol through AQbD to characterize the Protein Corona by minimizing errors due to data misinterpretation and by reducing and controlling lab-to-lab variability in order to better predict the PC consequences.

Methods

We have analyzed 90 articles devoted to PC characterization and revisited their contributions in the AQbD paradigm. The articles were selected according to the following criteria : published within the last years (2000-2019), published in English language and relevant with the search related terms.

Results

We have firstly proposed a generic analytical target profile of the PC characterization. We have also identified the critical biological and physicochemical properties to be controlled as well as the critical risk factors among all the protocol parameters. Then, we have reported the main analytic methods used to analyze the PC within their limits and advantages [4] , applied to NP. Finally, we have exposed how to best exploited data analysis derived from these methods according to AQbD requirements.

Conclusion

We have outlined which analytical techniques are the most suitable at developing efficient predictive tests to systematically identify and validate physicochemical and biochemical markers correlated to corona formation on Nanoparticles using the novel approach of Quality by Design (AQbD).

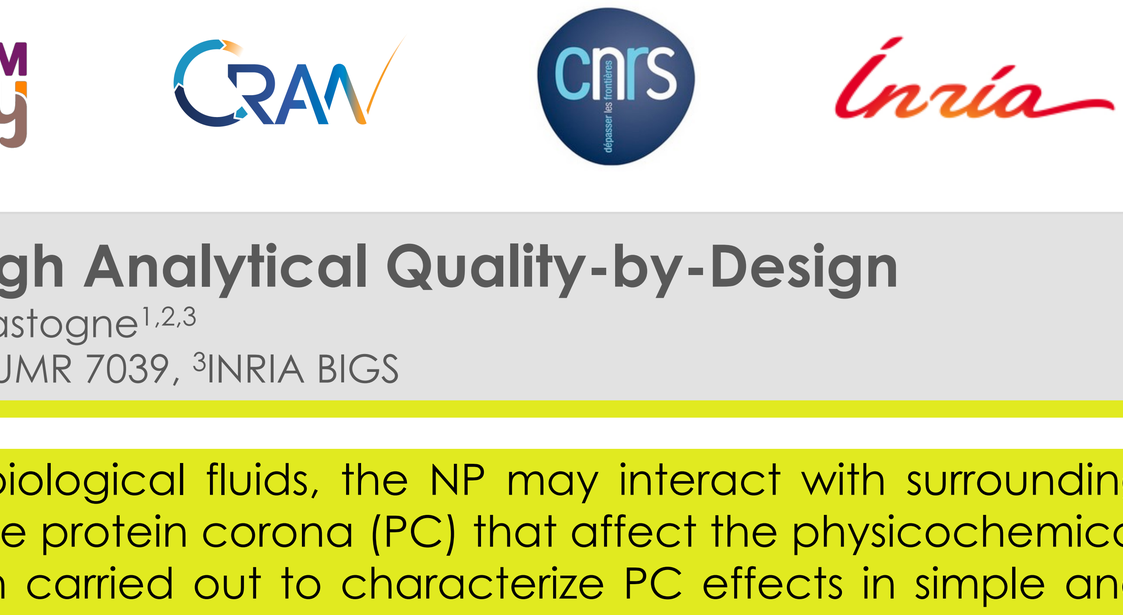

Fig.1: Schematic representation of dynamics exchanges of proteins forming the protein corona.

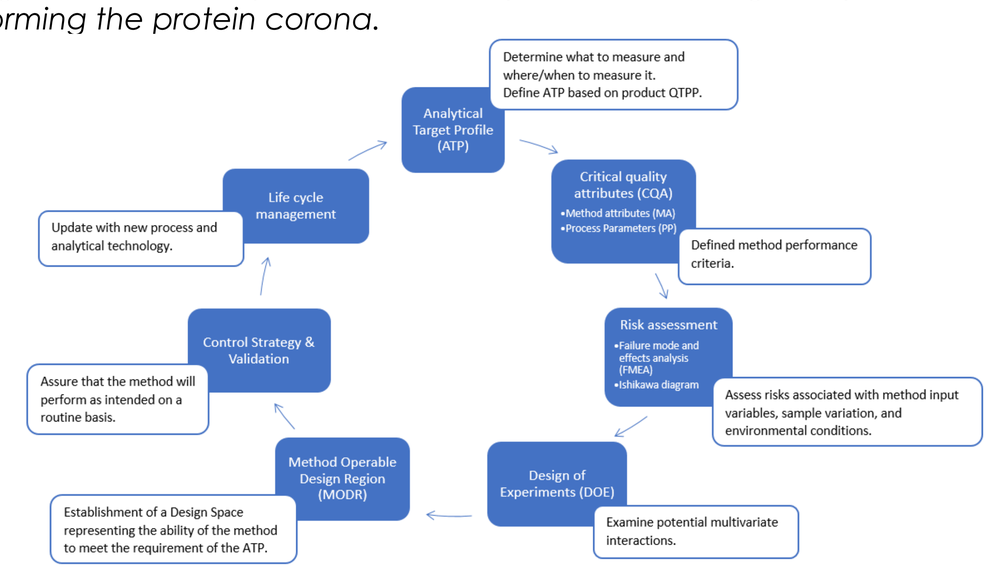

Fig.2: Analytical Quality by Design Workflow.

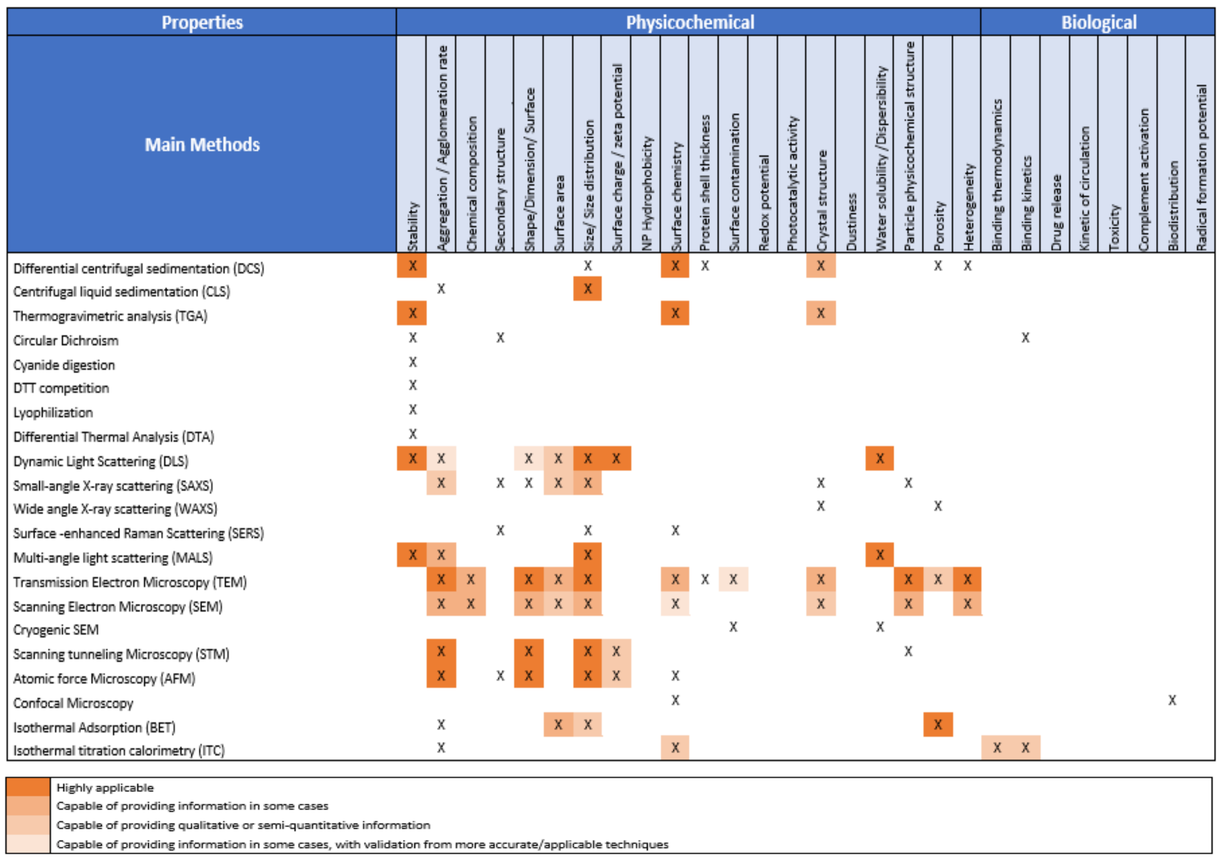

Fig.3: Presentation of some of the main methods to analyze physicochemical and biological properties of Nanoparticles.

References:
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